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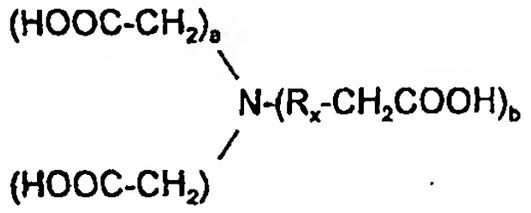

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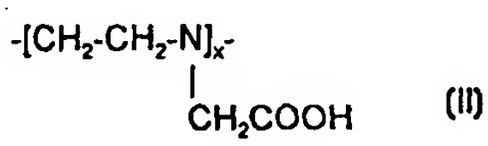

(II)

(57) Abstract

Disclosed is an antimicrobial composition containing about 0.1 to about 8.0 percent by weight of 2,4,4'–trichloro–2'–hydroxydiphenyl ether; about 0.1 to about 8.0 percent by weight of 4–chloro–3,5–dimethyl phenol; and about 0.025 to about 5.0 percent by weight of glutaraldehyde; wherein the composition provides antimicrobial properties to a handwash composition equivalent or superior to the antimicrobial properties of 50 ppm of available chlorine and has a pH from about 5.0 to about 11.0. Additionally disclosed is an antimicrobial composition additionally containing about 0.025 to about 8.0 percent by weight of a compound having structure (I) or a salt thereof wherein R_x is (II), x is 0–5, preferably 1–3; and a and b are independently 0, 1 or 2, provided that $2 \leq a+b \leq 3$. Also disclosed is a method of cleaning skin using these antimicrobial compositions.

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ANTIMICROBIAL COMPOSITION FOR HANDWASH AND A METHOD OF CLEANING SKIN USING THE SAME

Field of Invention

The present invention relates to antimicrobial compositions. In particular, the invention relates to liquid antimicrobial handwash compositions.

Background of Invention

There is a continuing need for mild and cost-effective cleaning compositions, particularly for use as skin cleansers. There is a more specific need for such compositions having antimicrobial properties. For example, in the food industry, the use of antimicrobial skin cleansers is commonplace as employees wash their hands throughout a work shift to avoid contamination of the food products. Antimicrobial skin cleanser compositions, especially liquid compositions, are also finding increased use in the consumer market, as consumers seek the added advantage of cleaning compositions having microbial properties.

Ideally, these skin cleanser compositions have optimal antimicrobial properties, mildness, smell, lather, performance, skin feel, stability, and cost. When the composition is a liquid, it is also desirable that it does not clog the tip of a liquid dispenser by solidifying on standing. Too often, however, one or more of these properties are sacrificed in favor of another property. For example, compositions designed for use in the food industry in the United States may be optimized to meet United States Department of Agriculture antimicrobial standards, with little regard to the qualities of mildness and smell.

The United States Department of Agriculture has classified liquid handsoaps and various sanitizing compositions into several classes in an effort to control the hand care of employees in the meat and poultry processing industry. Under this classification system, E2 represents the standard for handwashing and sanitizing compositions. E2-rated handwashing or sanitizing compositions have antibacterial efficacy equivalent to at least 50 ppm of available chlorine bleach. The food service industry

outside the United States employs a different method to evaluate the antimicrobial properties of the handwashing and sanitizing compositions used: a time-kill test. This time-kill test measures the *in vitro* ability of an antibacterial wash product to rapidly reduce a known population of bacteria. The time kill test under European test protocol refers to a bacterial reduction by a log of 3, i.e., 99.90% reduction using a composition at 50% dilution with a 30 second contact time.

Because of the importance of employee hand washing in the food and food service industries, these industries have adopted either standard for the hand washing products used by their employees. Products meeting these standards are effective in reducing or eliminating the pathogenic bacteria found on the hands of the employee. Pathogenic bacteria can be found on the hands after using a restroom, handling raw foods, or touching soiled surfaces. Proper hand washing with an effective antimicrobial soap is vital to prevent the transfer of these pathogenic bacteria to the cooked food items that will be served to the customer.

Pathogenic bacteria generally found on the hands of the food service employee includes both resident and transient microorganisms. A recent field study indicated that resident bacteria, those organisms that were found more than 75% of the time on the hands of the tested employees, include *Staphylococcus aureas*, a food borne pathogen that is usually buried deep within the pores of the skin. These resident bacteria are protected by the fatty secretions of the sebaceous glands and are not easily removed during hand washing. Transient bacteria, which appeared less than 25% of the time during the evaluations, are loosely attached to the skin surface and can easily cross contaminate food products if the employees do not wash their hands adequately. Transient bacteria, which include *Escherichia coli* and *Salmonella* species, can be found in varying levels of contamination. Low levels of contamination usually result from contact with raw food products of animal origin, while high levels generally result from improper hand washing after an employee's use of a restroom.

Therefore, a hand washing or sanitizing composition that removes both the resident and transient bacteria is necessary in the food service industry. However, even where a composition's antimicrobial properties were a primary concern, the prior art reveals little or no specific direction regarding the selection of particular combinations of antimicrobial ingredients to provide compositions that meet either the E2 antimicrobial standard or the time-kill standard while at the same time enhancing properties that maintain mildness, and that do not have a sustained medicinal odor.

U.S. Patent 5,480,586 discloses an aqueous dishwashing detergent which may contain antimicrobial agents. The '586 patent discloses that the detergent may contain trichlorohydroxydiphenyl ether in combination with a second antimicrobial agent selected from the group consisting of Formalin®, Glydant® Plus, Kathon®, and Dowicil® 75. No particular advantage resulting from any particular combination is described.

U.S. Patent 5,646,100 describes an aqueous liquid composition containing an anionic surfactant, a betaine, an alkyl polyglycoside, and a mixture of antibacterial agents. Although triclosan is listed as one antibacterial agent, the '100 patent provides no further guidance as to what mixtures of antibacterial agents should be used.

U.S. Patent 5,653,970 broadly relates to "personal care products" containing as many as 26 different ingredients. Listing many choices for those potential ingredients, the '970 patent also contains a substantial list of antimicrobial agents which happens to include glutaraldehyde, triclosan, and p-chloro-m-xylenol. The preferred antimicrobial agent is a combination of methyl isothiazoline and chloromethyl isothazoline sold under the trade name Kathon® CG. Kathon® CG is a preservative and is primarily used as such and could not be used as an antimicrobial agent.

U.S. Patent 5,681,802 relates to a liquid skin cleansing composition containing a mild surfactant system, a pH buffer, and an antibacterial agent. According to the '802 patent, the pH buffer and antibacterial agent potentiate the antimicrobial effect of the composition.

WO 95/09605 exemplifies an antibacterial liquid hand soap concentrate containing sodium lauryl sulfate, alkylpolyglucoside, coconut betaine, triclosan, propylene glycol, glycerine, and sodium chloride.

WO 96/29049 discloses liquid skin cleansing compositions and teaches that one or more polyvalent cations may be used to synergistically provide an antibacterial effect when used in mild, liquid skin cleansing compositions.

While commercially available products such as Purell®, Mircell®, Safeguard®, and Soft Soap® contain triclosan and may have a pleasant odor, those products do not meet antimicrobial efficacy requirements for use in the food service and food handling industry. Instead of providing antimicrobial properties at least equivalent to those of 50 ppm of available chlorine, the above-listed products are considered bacteriostatic only.

Thus, antimicrobial compositions used in cleaners typically fail to provide a broad spectrum of satisfactory properties. Those compositions that contain only triclosan as an antimicrobial may be odorless and effective against broad spectrum bacteria, but fail to provide substantial kill properties against gram negative bacteria such as Pseudomonas. The cost of triclosan containing products is also relatively high. Those compositions that contain only p-chloro-m-xylenol ("PCMX") as an antimicrobial may be effective against gram negative bacteria, but leave an undesirable and sustained medicinal odor, irritate the skin, and do not provide significant long term antimicrobial protection.

To date, no product that meets the antimicrobial efficacy requirements for use in the food service and food handling industry while at the same time providing acceptable mildness, smell, lather, performance, skin feel, stability, and cost is commercially available. The antimicrobial compositions according to the present invention for the first time possess the highly desirable combination of high antimicrobial efficacy, and optimal cost and improved mildness, smell, lather, performance, skin feel, and stability characteristics.

Objects of the Invention

An object of the present invention is to provide an improved composition having antimicrobial properties.

Another object of the present invention is to provide a composition that has an antimicrobial efficacy equivalent to at least 50 ppm of free chlorine bleach.

Another object of the present invention is to provide a composition that is mild and does not irritate or dry the skin after frequent use.

An additional object of the present invention is to provide a composition that does not clog the tip of a liquid dispenser by solidifying upon standing.

A further object of the invention is to provide a stable liquid composition that has a pleasant smell and does not leave a sustained medicinal odor on the hands or skin after use.

Additional objects and advantages of the present invention will be apparent from the description, or may be learned by practice of the invention. The objects and advantages of the invention will be realized by the elements and combinations particularly pointed out in the appended claims.

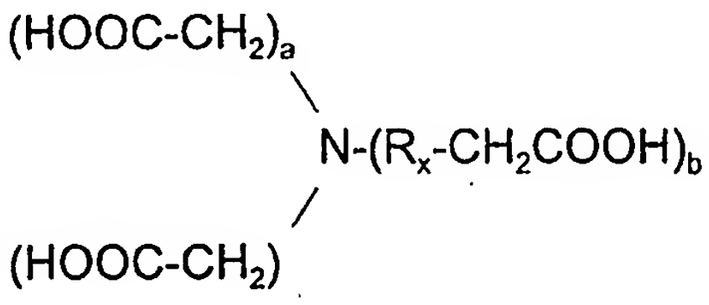
Summary of the Invention

To achieve these and other objectives, and in accordance with the purpose of our invention as embodied and broadly described herein, the present invention provides an antimicrobial composition comprising: (a) about 0.1 to about 8.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether; (b) about 0.1 to about 8.0 percent by weight of 4-chloro-3,5-dimethyl phenol; and (c) about 0.025 to about 5.0 percent by weight of glutaraldehyde; wherein the composition provides antimicrobial properties to a handwash composition equivalent or superior to the antimicrobial properties of 50 ppm of available chlorine.

It is also an object of the present invention to provide an antimicrobial composition comprising: (a) about 0.1 to about 8.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether; (b) about 0.1 to about 8.0 percent

by weight of 4-chloro-3,5-dimethyl phenol; (c) about 0.025 to about 5.0 percent by weight of glutaraldehyde; and (d) about 0.025 to about 8.0 percent by weight of compound having

the following structure or a salt thereof:



wherein R_x is $-[CH_2-CH_2-N]_x-$ with CH_2COOH

x is 0-5, preferably 1-3; and

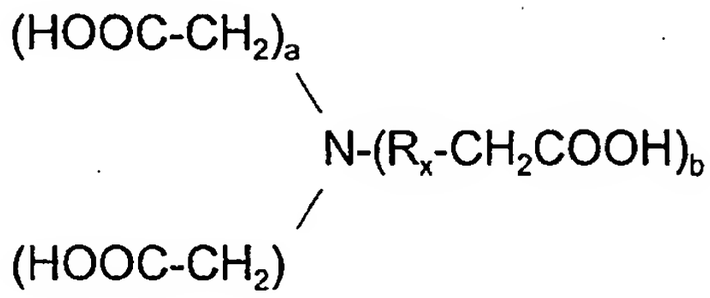
a and b are independently 0, 1 or 2, provided that $2 \leq a + b \leq 3$;

wherein the composition provides antimicrobial properties to a handwash composition equivalent or superior to the antimicrobial properties of 50 ppm of available chlorine.

It is yet another object of the present invention to provide a method of cleaning skin, in which a composition is contacted with the skin and the composition comprising: (a) a surfactant system including an anionic surfactant, a cationic surfactant, a nonionic surfactant, or an amphoteric surfactant, or any combination thereof; (b) about 0.1 to about 8.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether; (c) about 0.1 to about 8.0 percent by weight of 4-chloro-3,5-dimethyl phenol; and (d) about 0.025 to about 5.0 percent by weight of glutaraldehyde.

Finally, it is an object of the present invention to provide a method of cleaning skin, in which a composition is contacted with the skin and the composition comprises: (a) a surfactant system including an anionic surfactant, a cationic surfactant, a nonionic surfactant, or an amphoteric surfactant, or any combination thereof; (b) about 0.1 to about 8.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether; (c) about 0.1 to about 8.0 percent by weight of 4-chloro-3,5-dimethyl phenol; (d) about 0.025 to about 5.0 percent by weight of glutaraldehyde; and (e) about 0.025 to about 8.0

percent by weight of compound having the following structure or a salt thereof:



wherein R_x is $-[CH_2-CH_2-N]_x-$ with CH_2COOH on the nitrogen

x is 0-5, preferably 1-3; and

a and b are independently 0, 1 or 2, provided that $2 \leq a + b \leq 3$.

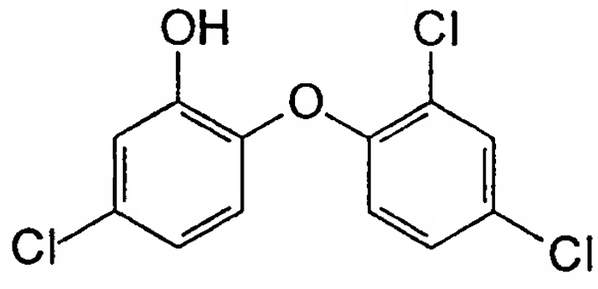
Detailed Description of the Invention

The "E2 antimicrobial" efficacy or standard refers to an antimicrobial kill property that is equivalent to or surpasses the efficacy of 50 ppm of available chlorine. The E2 standard is required by the United States Department of Agriculture for hand soaps used on site by employees in the meat and poultry processing industry and has been adopted by restaurant establishments in the United States. Preferably, antimicrobial compositions described herein have an antimicrobial efficacy equivalent to or greater than that of 200 ppm of available chlorine. A description of a test method used to determine whether a composition meets the E2 antimicrobial standard can be found in AOAC Official Method of Analysis No. 955.16, Official Methods of Analysis, 16th Ed. (1995), the entire contents of which are incorporated herein by reference.

Another test used to evaluate the antimicrobial properties of a composition is known as the time-kill test. In this test, the degree to which bacteria are killed when exposed to an antibacterial agent over time is recorded. In a time kill test, the test composition is diluted so that after addition of inoculum the test composition is at use concentration. The test composition is then brought into contact with a known population of test bacteria for a specified time period at a specified temperature. The antimicrobial ingredients are neutralized at the end of the time period and the sample is plated to enumerate the surviving bacteria. The percent reduction

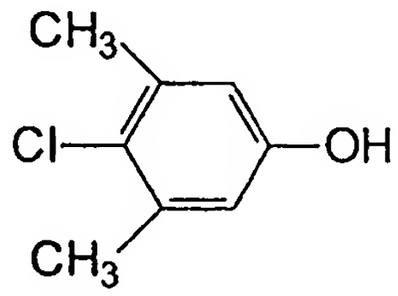
from the original population is then calculated. The proposed test method (U.S. Timekill Test) in the Healthcare Continuum submitted to the FDA requires a 60-second contact time of a 50% diluted composition resulting in greater than 1 log reduction (90%) in bacterial count. The European Time-kill test (pp EN12054, EN1499, 1997) is very similar. The European Time-kill test requires a 3 log reduction (99.9%) in a 60 or 30 second contact time of a 55% dilution of soap. Both the U.S. and European Time-kill tests are the proposed tests and have not yet been accepted or finalized.

Despite the difficulties encountered in the prior art, the inventor found that an antimicrobial composition that has a kill property of at least 50 ppm of available chlorine (the E2 antimicrobial standard) may be formulated by selection of a combination of antimicrobial ingredients. Importantly, the antimicrobial composition has a pleasant smell and does not act as a skin irritant. A composition of the invention contains 2, 4, 4'-trichloro-2'-hydroxydiphenyl ether (also known as triclosan and sold as Irgasan® and Irgasan DP 300®) having the following structural formula:



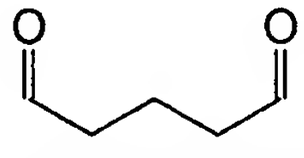
The triclosan may be present in the composition in an amount ranging from 0.1 to about 8.0 percent by weight, preferably about 0.2 to about 6.0 percent by weight, more preferably about 0.25 to about 4.0 percent by weight.

The composition also contains 4-chloro-3,5-dimethyl phenol (also known as PCMX and sold as Nipacide®) having the following structural formula:



The PCMX is present in the composition in an amount ranging from about 0.1 to about 8.0 percent by weight, preferably about 0.2 to about 6.0 percent by weight, more preferably about 0.25 to about 4.0 percent by weight.

The composition also contains glutaraldehyde, which has the following structural formula:

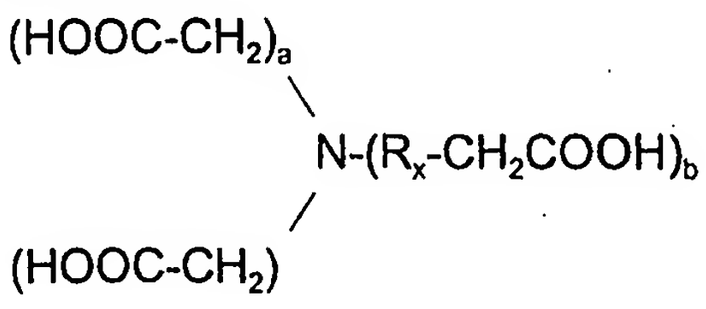


The glutaraldehyde is present in the composition in an amount ranging from about 0.025 to about 5.0 percent by weight, preferably about 0.05 to about 4.0 percent by weight, more preferably about 0.1 to about 3.0 percent by weight.

The antimicrobial ingredients according to the present invention are present in the composition in an amount of at least 1.25 percent by weight.

Surprisingly, it was found that this combination of antimicrobial ingredients, i.e., PCMX, triclosan, and glutaraldehyde, provides an improved and highly efficacious antimicrobial effect that meets or exceeds E2 antimicrobial efficacy. As a result, the composition may contain a lesser amount of PCMX in the composition while still maintaining antimicrobial efficacy that is equal to or surpasses that of 50 ppm of available chlorine. The presence of glutaraldehyde in the composition further enhances that antimicrobial effect, so that the combination of triclosan, PCMX, and glutaraldehyde is present in the composition in an amount effective to impart antimicrobial properties to a handwash composition equal to or surpassing that of 50 ppm of available chlorine.

It was also found that the antimicrobial properties of the composition can be still further enhanced by adding of a compound having the following structure or a salt thereof:



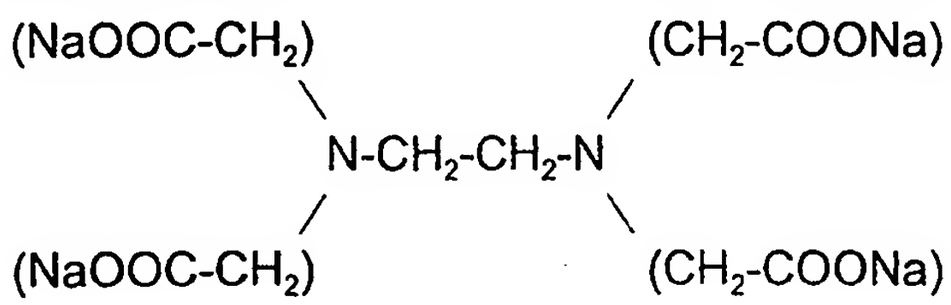
wherein R_x is $-[CH_2-CH_2-N]_x-$ with CH_2COOH on the nitrogen

x is 0-5, preferably 1-3; and

a and b are independently 0, 1 or 2, provided that $2 \leq a + b \leq 3$

The salts of the compound comprise those based on the Group IA metals (i.e., Li, Na, K, Rb, or Cs) or Group IIA alkaline earth metal carbonates (i.e., Be, Mg, Ca, Sr or Ba), ammonia, amines or hydroxylamines. The preferred salts comprise the alkali metal salts, especially the sodium salts.

More preferably, a, b and x are each 1, to provide ethylenediamine tetraacetic acid or a salt thereof (a.k.a. "EDTA") in the composition. Most preferably, a tetrasodium salt of ethylenediamine tetraacetic acid ("EDTA-Na_4") having the following formula is employed in the composition:



Accordingly, a preferred composition according to the present invention contains about 0.025 to about 8.0 percent by weight of the EDTA-Na_4 compound, more preferably about 0.05 to about 6.0 percent by weight, even more preferably about 0.1 to about 4.0 percent by weight. The total amount of antimicrobial ingredients, including EDTA-Na_4, present in the composition is at least 1.25 percent by weight.

Although PCMX is a strong antimicrobial agent and is effective against gram negative bacteria, PCMX imparts to the composition a strong and unpleasant medicinal odor. The enhanced antimicrobial properties provided by the presence of the above mentioned compound, for example EDTA-Na_4, however, advantageously allows one to formulate a composition having a reduced amount of PCMX. Thus, the composition has an improved fragrance and reduced skin irritation properties while still attaining an acceptable threshold level of antimicrobial properties.

When evaluating the composition according to the present invention using the time-kill standard, it was additionally found that the time-kill properties of the antibacterial compositions were greatly influenced by the pH of the composition. It was discovered that an antibacterial composition having a slightly alkaline pH possessed improved antimicrobial efficacy under a diluted concentration, e.g. 50% solution. Thus, a composition having a pH of about 5.0 to 11.0 is preferred. More preferrably, the pH of the compositions according to the present invention ranges from about 5.5 to 10.5. Most preferrably, the pH of the compositions ranges from about 7.5 to 9.5.

Preferably, the antimicrobial composition also contains a surfactant system to form, in one embodiment, a handwash. The surfactant system may include at least one surfactant selected from the group consisting of an anionic surfactant, a cationic surfactant, a nonionic surfactant, an amphoteric surfactant, and any combination thereof. Preferably, the surfactant or surfactants selected reduce skin irritation and are compatible with the triclosan, PCMX and, glutaraldehyde. More preferably, the surfactant or surfactants are also compatible with EDTA-Na_4. In one embodiment, a suitable surfactant system contains at least one anionic surfactant, at least one nonionic surfactant, and at least one amphoteric surfactant.

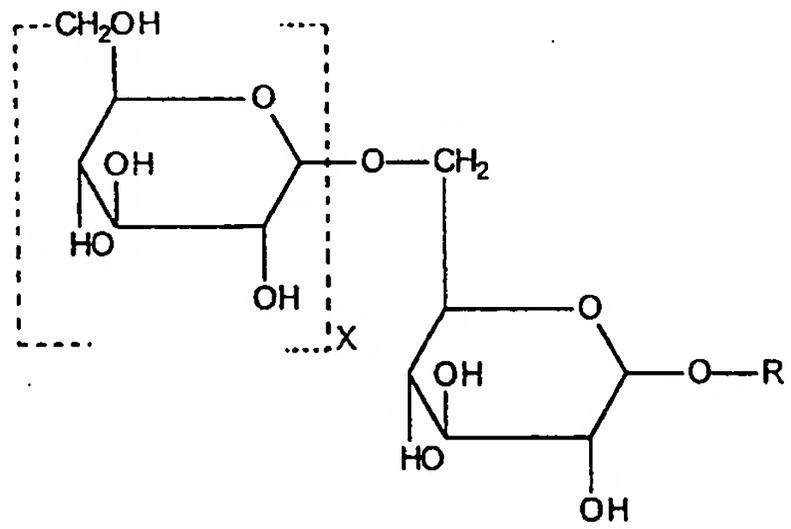
Anionic surfactants are typically used in skin cleansing compositions to provide deep skin cleaning properties, and sufficient lathering properties. Examples of anionic surfactants that may be used in the composition include alcohol sulfates; alcohol ether sulfates; fatty acid soaps such as sodium, potassium or ammonium salts of cocoates, tallowates, laurates, myristates, oleates, palmitates, etc.; α-olefin sulfonates; α-sulfomethyl esters, alkyl isethionates and sulfosuccinates. Preferred anionic surfactants include sodium lauryl ether sulfate (SLES), sodium lauriminodipropionate, sodium lauryl sulfate, ammonium lauryl sulfate, sodium cocoyl isethionate, sodium isethionate, sodium alkylbenzene sulfonate, sodium tallowate, sodium cocoate, sodium myristate, sodium oleate, disodium cocoamide monoethanol

amine sulfosuccinate, and disodium oleamido monoethanol amine sulfosuccinate.

More preferred anionic surfactants for use in the composition described herein include sodium lauryl ether sulfate with 2 to 4 moles of ethoxylation, sodium lauryl sulfate, and sodium C_{14}-C_{16} olefin sulfonate. Sodium lauryl ether sulfate-3EtO used in the composition may be obtained from Henkel Corporation under the tradenames Sulfotex® NL60S and Sulfotex® 6040S. Sodium lauryl sulfate may be obtained from Stepan Co. under the tradename Stepanol WAC® and also from Henkel under the tradename Standapol® WAQ. The anionic surfactant may be present in an amount ranging from about 1 to about 30 weight percent, preferably from about 1 to about 20 weight percent.

Nonionic surfactants that may be used in the composition include alkyl polyglycosides, alkyl glucamide or alkyl glucosamide and alkanol amides such as lauramide monoethanol amine, cocamide monoethanol amine, cocamide diethanol amine, and lauramide diethanol amine.

Preferred nonionic surfactants include polyglycosides such as alkyl polyglycosides. The alkyl polyglycosides have the following chemical structure:



in which R is an alkyl group having 8 to 16 carbon atoms, preferably 12 to 16 carbon atoms. When characterizing alkyl polyglycosides, the average number of glucose units per alkyl group is referred to as the degree of polymerization. A preferred degree of polymerization x for the alkyl polyglycoside used in the composition ranges from about 1 to about 10, more

preferably from about 1 to about 3. Examples of alkyl polyglycosides are fatty acid polyglycosides sold by Henkel Corporation under the tradename Glucopon®. Preferred alkyl polyglycosides are sold as Glucopon® 425N , Glucopon® 600, Glucopon® 625, and Glucopon® 200. The composition may include about 0 to about 20 weight percent of the nonionic surfactant, preferably about 1 to about 15 weight percent.

Preferred amphoteric surfactants include betaines such as cocoamidopropyl betaine and amphoacetates such as a glycine based sodium cocoamphoacetate, sodium lauroamphoacetate, and sodium cocoamphodiacetate. Commercially available betaines that may be used include Velvetex® BA-35 sold by Henkel Corporation, Amphosol® CA and Amphosol® CG sold by Stepan Co., Tego Betaines sold by Goldschmidt, Mackam® 35 sold by McIntyre and Mirataine® CB sold by Rhone-Poulenc. The amphoteric surfactant may be present in an amount ranging from about 0 to about 15 weight percent, preferably about 1 to about 10 weight percent.

As mentioned, a preferred composition contains at least one surfactant selected from the group consisting of an anionic surfactant, a nonionic surfactant, and an amphoteric surfactant or any combination thereof. In such a surfactant system, each surfactant is present in the amounts previously described for each. In this embodiment, the nonionic surfactant and the amphoteric surfactant are believed to raise the performance of the anionic surfactant, lower skin irritation, increase smooth skin feel, and increase the character of the lather.

The composition may also contain skin conditioning agents to provide a moisturizing effect and a soft skin feel. Examples of such skin conditioning agents include glycerine, propylene glycol, polyethylene glycol-7 glyceryl cocoate, copolymers of dimethyldiallylammonium chloride and acrylamide, hydrolyzed silk peptide, hydrolyzed silk protein, aloe vera gel, guar hydroxypropyltrimonium chloride, isostearamidopropyl morpholine lactate, stearic acid, fatty monoglyceride, cyclomethione, methyl glucose dioleate, and glycol distearate. PEG-7 glyceryl cocoate sold as Cetiol® HE by Henkel

Corporation and dimethylallylammonium chloride/acrylamide copolymers such as Mackernium® 007 sold by McIntyre Group Ltd. are preferred skin conditioning agents for the composition. The skin conditioning agent may be present in an amount ranging from about 0 to about 5 weight percent.

Thickeners may also be added to control the viscosity of the composition. Preferably, the composition contains a thickener in an amount to impart a viscosity to the composition ranging from about 250 to about 7000 cps, more preferably about 400 to about 6000 cps. Such thickeners include polymeric thickeners such as cellulose, polyacrylate, and polycarboxylic acids, and inorganic salt thickeners such as sodium chloride, potassium chloride, magnesium chloride, potassium sulfate, and sodium sulfate. The thickeners may be present in amounts ranging from about 0 to 5 weight percent preferably about 0.25 to about 4.5 weight percent, most preferably about 0.35 to about 3 weight percent.

Builders such as citric acid and sodium citrate, and any mixture thereof may also be included in the composition. Preferably, the builder is present in an amount ranging from about 0 to about 10 weight percent, more preferably from about 0.25 to about 5 weight percent.

Other conventional additives for cleaning compositions, particularly handwash compositions, may be used. For example, pearlescent agents such as stearic acid and glycol stearate may be used. Preservatives that may be used in the composition include DMDM hydantoin.

Examples of preferred compositions embraced by the invention are shown in Table 1.

Table 1

Ingredient	Weight Percent 138-55-1	Weight Percent 138-55-2
Nipacide PX-R (PCMX)	1.00	1.00
Irgasan DP-300 (Triclosan)	0.30	0.30
Propylene Glycol	1.00	1.00
Sulfotex NL-60S (60 wt% sodium lauryl ether sulfate)	8.00	8.00
Glucopon 425N (50 wt% alkyl polyglycoside)	8.00	8.00
Velvetex BA 35 (30 wt% cocamidopropyl betaine)	3.00	3.00
Standapol WAC (29 wt% sodium lauryl sulfate)	3.00	3.00
Hampene 100 (30 wt% EDTA-Na_4)	1.00	1.00
Citric Acid (50% solution)	0.20	0.20
Ucarcide 250 (50 wt% glutaraldehyde)	0.25	0.25
Cetiol HE (100 wt% PEG-7 glyceryl cocoate)	0.25	0.25
Mackernium 007 (100 wt% polyquaternium 7)	0.25	0.25
Soft water	72.95	73.04
Dye, FD&C Yellow #5	0.00015	0.00015
Dye, FD&C Red #33	0.00008	0.00008
Dye, FD&C Red #40	0.00030	0.00030
Sodium Chloride- Granular High Grade	0.70	0.70
Perfume SZ3109	0.10	--

When used in compositions formulated as liquid skin cleansers, it is desirable that the composition be mild to the skin and passes the primary skin irritation test, also known as the Draize test. A description of the Draize test can be found in Example 10 below.

EXAMPLE 1

PCMX and triclosan are relatively insoluble in water. For that reason, to form compositions containing PCMX and triclosan, a premix of PCMX, triclosan, sodium lauryl ether sulfate, and propylene glycol was formed. Sodium lauryl ether sulfate contains about 13-16% ethanol which helps dissolve PCMX and triclosan along with propylene glycol. Sodium lauryl sulfate and the remaining ingredients were added to the premix and the resulting mixture was stirred to create an homogenous composition. Table 2 below shows the contents of the resulting compositions.

Table 2

Ingredient	Weight Percent (38-1)	Weight Percent (38-2)
Nipacide PX-R (PCMX)	1.00	1.00
Irgasan DP-300 (Triclosan)	0.20	0.20
Sulfotex 6040 (60 wt% sodium lauryl ether sulfate)	8.00	8.00
Propylene glycol	1.30	1.30
Glucopon 425N (50 wt% alkyl polyglycoside)	5.00	5.00
Velvetex BA 35 (30 wt% cocamido propyl betaine)	3.00	3.00
Stepanol WAC (29 wt% sodium lauryl sulfate)	2.00	2.00
Cetiol HE (100 wt% PEG-7 glyceryl cocoate)	0.20	--
Hampene 100 (30 wt% EDTA-Na_4)	1.00	1.00
Ucarcide 250 (50 wt% glutaraldehyde)	0.20	0.20
Citric Acid (50 wt% solution)	0.20	0.20
Water	75.80	76.10
Sodium Chloride	1.00	1.00

The viscosities of the compositions were 780 and 900 cps, respectively, as measured by a Brookfield viscosimeter with a 20 rpm,

number 3 spindle. The pH of each composition was 6.4 and both compositions passed the E2 antimicrobial test.

EXAMPLE 2

Another composition that passed the E2 antimicrobial test is shown in Table 3 below:

Table 3

Ingredient	Weight Percent (36-1)
Sulfotex 6040 (60 wt% sodium lauryl ether sulfate)	10.00
Nipacide PX-R (PCMX)	1.20
Irgasan DP-300 (Triclosan)	0.20
Propylene Glycol	1.50
Glycerine	1.00
Glucopon 425N (50 wt% alkyl polyglycoside)	6.00
Stepanol WAC (29 wt% sodium lauryl sulfate)	1.00
Velvetex BA 35 (30 wt% cocamido propyl betaine)	3.00
Hampene 100 (30 wt% EDTA-Na_4)	1.00
Citric Acid (50 wt% solution)	0.20
Water	74.70
Sodium Chloride	0.20
Ucarcide 250 (50 wt% Glutaraldehyde)	0.20

EXAMPLE 3

The PCMX concentration in composition number 138-55-1 as shown in Table 1 was varied between 1.0 percent by weight and 0.5 percent by weight. The concentrations of the other components were maintained at the levels shown in Table 1. Each composition was tested for E2 antimicrobial-efficacy and the results are shown in Table 4.

Table 4

	138-55-1	138-55-2	138-55-3	138-55-4	138-55-5	138-55-6
PCMX, %	1.00	0.90	0.80	0.70	0.60	0.50
Triclosan, %	0.30	0.30	0.30	0.30	0.30	0.30
Glutaraldehyde (50%), %	0.25	0.25	0.25	0.25	0.25	0.25
EDTA-Na_4 (30%), %	1.00	1.00	1.00	1.00	1.00	1.00
E2 Antimicrobial Kill Test	Pass	Pass	Pass	Pass	Pass	Fail

The viscosity of each composition was adjusted to 1250 +/- 250 cps by the addition of sodium chloride. Citric acid (50%) was used to adjust the pH to 6.5-7.0. The target specific gravity was 1.022, and the compositions had a clear, peach color. Prototype 138-55-6 with 0.50% PCMX and 0.3% triclosan failed the E2 test because of low level of antimicrobial agents, an amount less than 1.25 percent by weight. This is an excellent example to show that by increasing EDTA-Na_4, the inventor was able to lower the PCMX concentration by 50% and still meet E2 efficacy. Formulation 138-55-6 contained only 1% EDTA-Na_4 (0.30% active concentration) and its EDTA-Na_4 concentration was not enough to further boost the kill property of the lower level of PCMX to meet E2 efficacy. On the other hand, by increasing the EDTA-Na_4 to 3% (0.90% active concentration), a formulation identical to 138-55-6 with the exception of the increased amount of EDTA-Na_4 passed the 30 seconds time kill test easily (5 bacterial log reduction). (See Table 7, prototype 1.) Thus, the increased EDTA-Na_4 efficiently compensated for the low level of PCMX to pass the kill test. A 50% reduction of PCMX and 3x increase of EDTA-Na_4 resulted in a savings of about 5-8% in formulation cost.

EXAMPLE 4

The compositions shown in Table 5 were evaluated to observe the effects of omitting alkyl polyglycoside, α-olefin sulfonate, betaine, or lauroamphoacetate surfactants from the composition. All of the compositions shown in Table 5 passed the E2 antimicrobial test. Thus, E2 antimicrobial efficacy is independent of the particular surfactant combinations described herein. Additional examples are provided in Table 14.

Table 5

Ingredients	Control	Prototype 1	Prototype 2	Prototype 3	Prototype 4
Propylene Glycol	1.00	1.00	1.00	1.00	1.00
PCMX	1.00	1.00	1.00	1.00	1.00
Triclosan	0.30	0.30	0.30	0.30	0.30
Sulfotex NL-60S (60% SLES)	8.00	8.00	8.00	8.00	8.00
Glucopon 425 (50% APG)	8.00	--	--	--	--
Na α-Olefin Sulfonate (Bio-Terge AS 40,40%)	--	8.00	8.00	8.00	6.00
Cocamidopropyl Betaine (35%)	3.00	--	--	3.00	2.00
Na lauroamphoacetate (Miranol HMA, 30%)	--	3.00	3.00	--	3.00
Sodium Lauryl Sulfate (29%)	3.00	3.00	3.00	3.00	3.00
EDTA-Na_4 (30%)	1.00	1.00	1.00	1.00	1.00
PEG-7 Cocoyl Glycerate	0.25	0.25	0.25	0.25	0.25
Polyquaternium 7	0.25	0.25	0.25	0.25	0.25
Glutaraldehyde (Ucarcide 250, 50%)	0.25	0.25	0.25	0.25	0.25
Citric Acid (50%)	0.20	0.20	0.20	0.20	0.20
NaCl	0.40	0.40	0.40	0.40	0.40
Water, Perfume, Dyes, etc.	qs	qs	qs	qs	qs

EXAMPLE 5

The following compositions in Table 6 were formulated and the antimicrobial properties of each was evaluated by an antimicrobial time-kill

test method. The time-kill test method measures the *in vitro* ability of the antimicrobial composition to rapidly reduce a known population of bacteria. A 50% dilution of each composition was brought into contact with a known population of test bacterial for a specified period of time (30 seconds) at a specified temperature. The antimicrobial ingredients were neutralized at the end of the test period and the sample was plated to enumerate the surviving bacteria. The percent reduction from the original population was calculated.

Table 6

Ingredients	Control	Prototype 1	Prototype 2	Prototype 3	Prototype 4	Prototype 5	Prototype 6	Prototype 7
Propylene Glycol	1.00	2.00	3.00	1.00	2.00	3.00	1.00	2.00
PCMX	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Triclosan	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
Sufotex NL-60S (60% SLES)	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00
Glucopon 425 (50%)	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00
Cocamidopropyl Betaine (35%)	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
Sodium Lauryl Sulfate (29%)	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
EDTA-Na_4 (30%)	1.00	1.00	1.00	2.00	2.00	2.00	3.00	3.00
PEG-7 Cocoyl Glycerate	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Polyquaternium 7	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Glutaraldehyde (Ucarcide 250, 50%)	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Citric Acid (50%)	0.20	0.35	0.35	0.35	0.35	0.20	0.35	0.35
NaCl	0.40	--	--	--	--	--	--	--
Water, Perfume, Dyes, etc.	qs	qs	qs	qs	qs	qs	qs	qs
30 Seconds-50% Dilution Test (one log or 90% Reduction Required)	Borderline Pass	Borderline Pass	Borderline Pass	Borderline Pass	Borderline Pass	Borderline Pass	99.9995% (-5 log)	99.9995% (-5 log)

As can be seen in Table 6, all of the compositions resulted in a "borderline pass, i.e., about an 88 to 89 percent reduction in bacteria in the 30 second test. A comparison of the results attained by Prototypes 3 and 6 shows that increasing the EDTA-Na_4 concentration from 2.00 to 3.00 percent by weight provided a substantial increase in bacteria reduction. Similarly, a comparison of the results attained by Prototypes 4 and 7 also shows that increasing the EDTA-Na_4 concentration from 2.00 to 3.00 percent by weight provided a substantial increase in bacteria reduction. On the other hand, the increase of the EDTA-Na_4 concentration from 1.00 to 2.00 percent by weight in prototypes 1 and 4 provided no substantial increase in bacteria reduction.

As also shown by Table 6, increasing the concentration of propylene glycol from 1.00 to 3.00 percent by weight had no apparent effect on the antimicrobial properties of the composition, as measured by the 30 second time kill test.

EXAMPLE 6

The compositions in the following Table 7 were evaluated for antimicrobial properties by the same 30 second time kill test used in Example 5. As can be seen in Table 7, use of 3.00 percent by weight of EDTA-Na_4 in combination with PCMX concentrations down to 0.50 percent by weight (Prototype 1) resulted in 99.9995 percent bacteria reductions.

TABLE 7

Ingredients	Control	Prototype 1	Prototype 2	Prototype 3	Prototype 4	Prototype 5
Propylene Glycol	1.00	1.00	1.00	1.00	1.00	1.00
PCMX	1.00	0.50	0.60	0.70	0.80	0.90
Triclosan	0.30	0.30	0.30	0.30	0.30	0.30
SLES-Sulfotex NL-60S (60%)	8.00	8.00	8.00	8.00	8.00	8.00
Glucopon 425 (50%)	8.00	8.00	8.00	8.00	8.00	8.00
Cocamidopropyl Betaine (35%)	3.00	3.00	3.00	3.00	3.00	3.00
Sodium Lauryl Sulfate (29%)	3.00	3.00	3.00	3.00	3.00	3.00
EDTA-Na_4 (30%)	1.00	3.00	3.00	3.00	3.00	3.00
PEG-7 Cocoyl Glycerate	0.25	0.25	0.25	0.25	0.25	0.25
Polyquaternium 7	0.25	0.25	0.25	0.25	0.25	0.25
Glutaraldehyde (Ucarcide 250, 50%)	0.25	0.25	0.25	0.25	0.25	0.25
Citric Acid (50%)	0.20	0.35	0.35	0.35	0.35	0.35
NaCl	0.40	--	--	--	--	--
Water, Perfume, Dyes, etc.	qs	qs	qs	qs	qs	qs
30 Seconds - 50% Dilution Kill Test (one log or 90% Reduction Required)	Borderline Pass	Pass 5 log Red.	Pass 5 log Red.	Pass 5 log Red.	Pass 5 log Red.	Pass 5 log Red.

EXAMPLE 7

The compositions shown below in Table 8 were evaluated by the 30 second time kill test to observe the effect that the composition's pH has on antibacterial activity. All of the compositions shown in Table 8 which had a pH of 7.5 or greater passed the 50% diluted 30 second time-kill test.

Table 8

Ingredients	Control	Prototype 1	Prototype 2	Prototype 3	Prototype 4	Prototype 5	Prototype 6	Prototype 7	Prototype 8	Prototype 9	Prototype 10
Propylene Glycol	1.00	2.00	3.00	1.00	2.00	3.00	1.00	2.00	2.00	2.00	2.00
PCMX	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Triclosan	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
Sulfotex NL-60S (60% SLES)	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00
Glucopon 425 (50%)	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00	8.00
Cocamidopropyl Betaine (35%)	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
Sodium Lauryl Sulfate (29%)	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
EDTA-Na_4 (30%)	1.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
PEG-7 Cocoyl Glycerate	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Polyquaternium 7	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Glutaraldehyde (Ucarcide 250, 50%)	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Citric Acid (50%)	0.20	0.64	0.58	0.52	0.50	0.48	0.45	0.42	0.37	0.30	0.00
NaCl	0.40	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
Water, Perfume, Dyes, etc.	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
Viscosity, cps (20 rpm, #3 spindle)	1250	540	550	555	555	565	555	560	570	559	840
570pH (Neat Solution)	6.70	6.50	6.75	7.00	7.25	7.50	7.75	8.00	8.25	8.50	9.50
30 Seconds-50% Dilution Test	Borderline Pass	Fail	Fail	Fail	Fail	Pass	Pass	Pass	Pass	Pass	Pass

EXAMPLE 8

The compositions shown below in Table 9 were evaluated by both the E2 antimicrobial test and the 30 second time-kill test to observe the effects of omitting alkyl polyglycoside, α-olefin sulfonate, betaine, or lauroamphoacetate surfactants from the composition. All of the compositions shown in Table 8 passed the E2 antimicrobial test and provided a 99.9995 percent bacteria reduction in the 30 second time kill test. Thus, the antimicrobial efficacy of the listed compositions having only 0.5 percent by weight PCMX (examples/prototypes 1-4) is independent of the particular surfactant combinations described herein.

Table 9

Ingredients	Control	Prototype 1	Prototype 2	Prototype 3	Prototype 4
Propylene Glycol	1.00	1.00	1.00	1.00	1.00
PCMX	1.00	0.50	0.50	0.50	0.50
Triclosan	0.30	0.30	0.30	0.30	0.30
Sulfotex NL-60S (60% SLES)	8.00	6.00	6.00	8.00	6.00
Glucopon 425 (50%)	8.00	2.00	2.00	2.00	2.00
Na α-Olefin Sulfonate (Bio-Terge AS 40, 40%)	--	6.00	6.00	6.00	6.00
Cocamidopropyl Betaine (30%)	3.00	--	--	3.00	1.50
Na Lauroamphoacetate (Miranol HMA, 30%)	--	3.00	3.00	--	1.50
Sodium Lauryl sulfate (29%)	3.00	3.00	3.00	3.00	3.00
EDTA-Na_4 (30%)	1.00	3.00	3.00	3.00	3.00
PEG-7 Cocoyl Glycerate	0.25	0.25	0.25	0.25	0.25
Polyquaternium 7	0.25	0.25	0.25	0.25	0.25
Glutaraldehyde (Ucarcide 250, 50%)	0.25	0.25	0.25	0.25	0.25
Citric Acid (50%)	0.20	0.20	0.20	0.20	0.20
NaCl	0.40	0.70	0.70	0.70	0.70
Water, Perfume, Dyes, etc.	qs	qs	qs	qs	qs
E-2 Kill Test	Pass	Pass	Pass	Pass	Pass
30 Seconds - 50% Dilution Kill Test	Borderline Pass	5 Log Red.	5 Log Red.	5 Log Red.	5 Log Red.

EXAMPLE 9

The relationship between sodium chloride content and viscosity was studied by varying the amounts of sodium chloride in composition number 138-55-1. The following viscosities and appearances were observed.

Table 10

	NaCl, %	Viscosity, cps	Appearance
138-58-1	0.00	280	Clear
138-58-2	0.35	1000	Clear
138-58-3	0.40	1365	Clear
138-58-4	0.45	1325	Clear
138-58-5	0.50	1355	Clear
138-58-6	0.55	1280	Clear
138-58-7	0.60	1175	Clear
138-58-8	0.65	1025	Clear
138-58-9	0.70	945	Slight Haze
138-58-10	0.75	865	Haze
138-58-11	0.80	720	Haze
138-58-12	0.85	615	Haze
138-58-13	0.90	540	Haze

EXAMPLE 10

Composition number 138-55-1 of Table 1 was tested to provide information on any skin irritation arising from a single 4 hour exposure by the dermal route.

A group of New Zealand albino rabbits was received from Davidson's Mill Farm, South Brunswick, N.J. The animals were singly housed in suspended stainless steel caging with mesh floors. Litter paper was placed beneath the cages and was changed at least three times per week. The animal room was temperature controlled and had a 12-hour light/dark cycle. The animals were fed Purina Rabbit Chow #5326 and filtered tap water was supplied *ad libitum* by automatic watering system.

Following acclimation to the laboratory, a group of animals was prepared by clipping (Oster model #A2-small) the dorsal area of each animal's trunk free of hair. On the day after clipping, six healthy rabbits (4 male and 2 females) without pre-existing dermal irritation were selected for test. One intact test site, approximately 6 cm^2, was delineated on each animal.

Five-tenths of a milliliter of the composition was applied to each dose site and covered with a 1" x 1", 4-ply gauze pad. The pad and entire trunk of each animal were then wrapped with semi-occlusive 3" Micropore tape to avoid dislocation of the pad. Elizabethan collars were placed on each rabbit and they were returned to their designated cages.

After 4 hours of exposure to the test substance, the patches and collars were removed and the test sites gently wiped with water and a clean towel to remove any residual test substance. Individual dose sites were scored according to the Draize scoring system, described in Draize et al., "Methods for the study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," J. Pharmacol. Exp. Ther., 1944; 82:377-90, the entire contents of which are incorporated herein by reference, at approximately 1, 24, 48, and 72 hours after patch removal.

The classification of irritancy was obtained by adding the average erythema and edema scores for the 1, 24, 48 and 72 hour scoring intervals and dividing by the number of evaluation intervals (4).

The resulting Primary Dermal Irritation Index (PDII) was classified as follows:

PDII	Classification
Less than 2.0	Slightly irritating
2.0-5.0	Moderately irritating
Greater than 5.0	Severely irritating

All animals appeared active and healthy. Apart from the skin irritation noted below, there were no signs of gross toxicity, adverse pharmacologic effects or abnormal behavior.

Within one hour of patch removal, very slight edema and/or very slight to well-defined erythema were noted at all treated sites. The incidence and severity of irritation decreased with time. By 72 hours, all rabbits were free of dermal irritation.

The Primary Dermal Irritation Index (PDII) for tested composition is 1.0. Based on the scoring and classification system used, the tested composition is slightly irritating to the skin of rabbits when applied.

EXAMPLE 11

Composition number 138-55-1 of Table 1 was tested to provide information on any eye irritation arising from a single instillation of the composition into the eye of one rabbit.

A group of New Zealand albino rabbits was received from Davidson's Mill Farm, South Brunswick, N.J. The animals were singly housed in suspended stainless steel caging with mesh floors. Litter paper was placed beneath the cages and was changed at least three times per week. The animal room was temperature controlled and had a 12-hour light/dark cycle. The animals were fed Purina Rabbit Chow #5326 and filtered tap water was supplied *ad libitum* by automatic watering system.

Following acclimation to the laboratory, the eyes of the above group of animals were examined. One healthy rabbit (male) without pre-existing ocular irritation was selected for test. One-tenth of a milliliter of the test substance was then instilled into the conjunctival sac of the right eye of this rabbit by pulling the lower lid away from the eyeball. The upper and lower lids were gently held together to about 1 second before releasing, to minimize loss of the test substance. The left eye remained untreated with the test substance and served as a control.

Ocular irritation was evaluated with the illumination of a white light source at 1, 24, 48, and 72 hours after instillation according to the method described in Draize et al., "Methods for the study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," J. Pharmacol. Exp. Ther., 1944; 82:377-90, the entire contents of which have

previously been incorporated herein by reference. Fluorescein dye (2% fluorescein sodium) was used at 24 hours and as needed at subsequent scoring intervals to evaluate the extent of corneal damage or to verify reversal of effects. The animal's score at the 24 hour interval was used to further classify the test substance by the system described in Kay et al., "Interpretation of Eye Irritation Tests," J. Soc. Cos. Chem., 1962; 13:281-89, the entire contents of which are incorporated herein by reference.

The rabbit appeared active and healthy. Apart from the eye irritation noted below, there were no other signs of gross toxicity, adverse pharmacologic effects or abnormal behavior.

Within 24 hours of test substance instillation, the treated eye exhibited corneal opacity and conjunctivitis, which persisted through 48 hours. The rabbit was free of ocular irritation within 72 hours (termination).

Based on the scoring system used, the 24 hour score of the tested composition is 17.0. That score classifies the test substance instilled in one eye as mildly irritating to the eye. Five animals are needed to obtain a definitive classification.

COMPARATIVE EXAMPLE 1

Compositions containing PCMX and triclosan as antimicrobial agents were prepared as shown in the following Table 11:

Table 11

Ingredient	Weight Percent (138-26-2)	Weight Percent (138-26-1)
Water	76.00	74.50
Sodium Chloride	1.00	1.00
Nipacide PX-R (PCMX)	1.00	1.00
Irgasan DP-300 (Triclosan)	0.20	0.20
Propylene glycol	1.50	1.50
Steol CS 460 (60% SLES)	4.00	4.00
Glucopon 425N (50 wt% alkyl polyglycoside-)	5.00	5.00
Velvetex BA 35 (30 wt% cocamido propyl betaine-)	6.00	6.00
Stepanol WAC (29 wt% sodium lauryl sulfate)	4.00	4.00
Citric acid (50% solution)	0.20	0.20
Perfume	0.10	0.10
Hampene 100 (30% EDTA-Na_4)	1.00	1.00
Cetiol HE (100 wt% PEG-7 glyceryl cocoate)	--	0.50
Mackernium 007 (100 wt% polyquaternium 7)	--	0.50
Hi Care (Guar hydroxypropyltrimonium chloride)	--	0.25

The viscosity of composition number 138-26-2 was 5000 cps, as measured by a Brookfield viscometer at 20 rpm with a number 3 spindle. The viscosity of composition 138-26-1 was 450 cps, and the composition was observed to be cloudy or milky.

The compositions of Table 11 were subjected to the E-2 test method to determine whether the antimicrobial efficacy of each composition was equivalent to or surpassed that of 50 ppm of free chlorine. The compositions, which contained no glutaraldehyde, did not show consistent results, as

composition number 138-26-2 failed the E-2 test and composition 138-26-1 passed the E2 test.

COMPARATIVE EXAMPLE 2

Compositions containing PCMX and triclosan as antimicrobial agents were prepared as shown in the following Table 12:

Table 12

Ingredient	Weight Percent (34-4)	Weight Percent (34-5)	Weight Percent (35-3)	Weight Percent (35-4)
Water	72.90	73.40	71.40	70.40
Cellocize QP 4400	0.50	--	--	0.70
Hampene 100 (30% EDTA-Na_4)	1.00	1.00	1.00	1.00
Stepanol WAC (29 wt% sodium lauryl sulfate)	12.0	12.00	10.00	10.00
Glucopon 425N (50 wt% alkyl polyglycoside)	4.00	4.00	6.00	6.00
Velvetex BA 35 (35 wt% cocamido propyl betaine-)	3.00	3.00	3.00	3.00
Citric acid (50% solution)	0.20	0.20	0.20	0.20
Nipacide PX-R (PCMX)	1.20	1.20	1.20	1.20
Irgasan DP-300 (Triclosan)	0.20	0.20	0.20	0.20
Ethanol	3.00	3.00	5.00	5.00
Propylene glycol	1.00	1.00	1.00	1.00
Glycerine	1.00	1.00	1.00	1.00

Only composition number 34-4 passed the E2 test method for antimicrobial efficacy. The other compositions shown in Table 12 failed, indicating that the combination of 1.2 weight percent PCMX and 0.2 weight percent triclosan in the above compositions did not consistently pass the E2 test in the absence of glutaraldehyde.

COMPARATIVE EXAMPLE 3

Table 13

Ingredient	Weight Percent (24-2)	Weight Percent (24-3)	Weight Percent (24-8)	Weight Percent (24-10)	Weight Percent (24-11)
Water	75.60	76.80	75.80	--	--
Cellocize QP 4400	0.10	0.10	0.10	--	--
Jaguar C-162	0.10	0.10	0.10	--	--
Hampene 100 (30% EDTA-Na_4)	1.00	1.00	1.00	--	--
Nipacide PX-R (PCMX)	1.00	1.00	1.00	1.00	1.00
Irgasan DP-300 (Triclosan)	0.20	0.20	0.20	0.20	0.20
Propylene glycol	1.50	1.50	1.50	--	--
Glycerine	1.00	1.00	1.00	--	--
Glucopon 425N (50 wt% alkyl polyglycoside)	5.00	5.00	5.00	5.50	6.50
Velvetex BA 35 (35 wt% cocamido propyl betaine)	6.00	6.00	6.00	8.50	9.00
Stepanol WAC (29 wt% sodium lauryl sulfate)	4.00	3.00	4.00	--	4.00
Citric Acid (50%)	0.30	0.20	0.15	--	--

When evaluated by the E2 test method, all of the compositions listed in Table 13, which contained no glutaraldehyde, failed to exhibit antimicrobial efficacy equivalent to 50 ppm of free chlorine.

EXAMPLE 12

The compositions shown in Table 14 were evaluated to observe the effects of omitting alkyl polyglycoside, α-olefin sulfonate, betaine, or lauroamphoacetate surfactants from the composition. All of the prototypes shown in Table 14 passed both the E2 antimicrobial test and the time-kill test.

It will be apparent to those skilled in the art that modifications and variations can be made in the novel composition of matter and process described herein without departing from the spirit or scope of the invention. It is intended that these modifications and variations and their equivalents are

to be included as part of this invention, provided they come within the scope of the appended claims.

Table 14

Ingredients	Control	Prototype 1	Prototype 2	Prototype 3	Prototype 4
PCMX	1.00	0.50	0.50	0.50	0.50
Triclosan	0.30	0.30	0.30	0.30	0.30
Propylene Glycol	1.00	--	--	--	--
Sulfotex NL-60S (60% SLES)	8.00	8.00	8.00	8.00	8.00
Glucopon 425N (50% APG)	8.00	8.00	8.00	--	--
α-Olefin Sulfonate (Bio-Terge AS 40, 40%)	--	--	--	8.00	8.00
Cocamidopropyl Betaine (35%)	3.00	3.00	--	3.00	--
(Na Lauroamphoacetate (Miranol HMA, 30%)	--	--	3.00	--	3.00
Sodium Lauryl SO_4 (29%)	3.00	3.00	3.00	3.00	3.00
EDTA-NA_4 (30%)	1.00	3.00	3.00	3.00	3.00
Cetiol HE	0.25	0.25	0.25	0.25	0.25
Polyquaternium 7	0.25	0.25	0.25	0.25	0.25
Glutaraldehyde (Ucarcide 250, 50%)	0.25	0.25	0.25	0.25	0.25
Perfume	0.10	0.10	0.10	0.10	0.10
Citric Acid (50%)	0.20	0.40	0.40	0.40	0.40
NaCl	0.80	1.20	1.60	1.60	1.60
Viscosity	1200	1150	1250	1200	2110
pH	6.5	8.5	8.5	8.5	8.5

What is claimed is:

1. An antimicrobial composition comprising:

(a) about 0.1 to about 8.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.1 to about 8.0 percent by weight of 4-chloro-3,5-dimethyl phenol; and

(c) about 0.025 to about 5.0 percent by weight of glutaraldehyde;

wherein at least 1.25 percent by weight of the combination of antimicrobial ingredients (a), (b) and (c) is present in the composition, and further wherein the composition provides antimicrobial properties to a handwash composition equivalent or superior to the antimicrobial properties of 50 ppm of available chlorine.

2. The antimicrobial composition of claim 1, comprising:

(a) about 0.2 to about 6.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.2 to about 6.0 percent by weight of 4-chloro-3,5-dimethyl phenol; and

(c) about 0.05 to about 4.0 percent by weight of glutaraldehyde.

3. The antimicrobial composition of claim 2, comprising:

(a) about 0.25 to about 4.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.25 to about 4.0 percent by weight of 4-chloro-3,5-dimethyl phenol; and

(c) about 0.1 to about 3.0 percent by weight of glutaraldehyde.

4. The antimicrobial composition of claim 1, further comprising at least one surfactant.

5. The antimicrobial composition of claim 4, further comprising at least one surfactant selected from the group consisting of an anionic surfactant, a nonionic surfactant, a amphoteric surfactant and any combination thereof.

6. The antimicrobial composition of claim 5, further comprising at least one anionic surfactant selected from the group consisting of an alcohol ether sulfate with 2 to 4 moles of ethoxylation, sodium lauryl sulfate, sodium α-olefin sulfonate, alkali fatty acid soap, sulfosuccinate, α-sulfomethyl ester, and fatty acylisethionate.

7. The antimicrobial composition of claim 5, further comprising at least one alkyl polyglycoside as the nonionic surfactant.

8. The antimicrobial composition of claim 5, further comprising at least one betaine or at least one amphoacetate as the amphoteric surfactant.

9. The antimicrobial composition of claim 5, further comprising about 1 to about 30 weight percent of the anionic surfactant, about 1 to about 20 weight percent of the nonionic surfactant, and about 0.5 to about 10 weight percent of the amphoteric surfactant.

10. The antimicrobial composition of claim 1, further comprising at least one skin conditioning agent.

11. The antimicrobial composition of claim 1, further comprising at least one thickener.

12. The antimicrobial composition of claim 1, wherein the composition is a liquid.

13. The antimicrobial composition of claim 1, wherein the composition is an aqueous liquid.

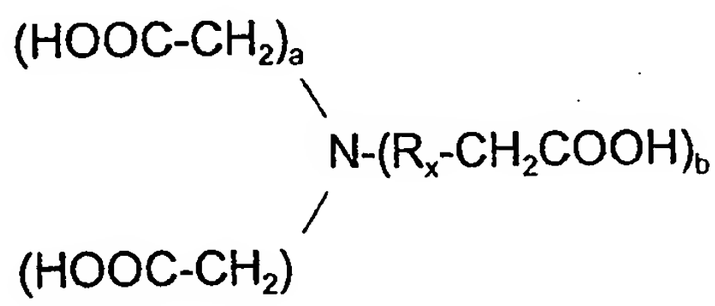
14. An antimicrobial composition comprising:

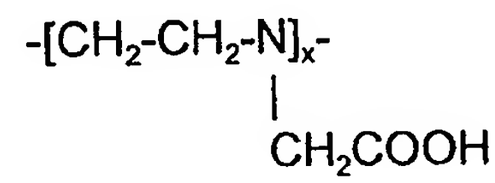
(a) about 0.1 to about 8.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.1 to about 8.0 percent by weight of 4-chloro-3,5-dimethyl phenol;

(c) about 0.025 to about 5.0 percent by weight of glutaraldehyde; and

(d) about 0.025 to about 8.0 percent by weight of a compound having the following structure or a salt thereof:



wherein R_x is 

x is 0-5, preferably 1-3; and

a and b are independently 0, 1 or 2, provided that $2 \leq a + b \leq 3$;

wherein at least 1.25 percent by weight of the combination of antimicrobial ingredients (a), (b) (c) and (d) is present in the composition, and further wherein the composition provides antimicrobial properties to a handwash composition equivalent or superior to the antimicrobial properties of 50 ppm of available chlorine.

15. The antimicrobial composition of claim 14, wherein component (d) is a tetrasodium salt of ethylenediameine tetraacetic acid.

16. The antimicrobial composition of claim 14, comprising:

(a) about 0.2 to about 6.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.2 to about 6.0 percent by weight of 4-chloro-3,5-dimethyl phenol;

(c) about 0.05 to about 4.0 percent by weight of glutaraldehyde; and

(d) about 0.05 to about 6.0 percent by weight of a tetrasodium salt of ethylenediameine tetraacetic acid.

17. The antimicrobial composition of claim 16, comprising:

(a) about 0.25 to about 4.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.25 to about 4.0 percent by weight of 4-chloro-3,5-dimethyl phenol;

(c) about 0.1 to about 3.0 percent by weight of glutaraldehyde; and

(d) about 0.1 to about 4.0 percent by weight of a tetrasodium salt of ethylenediameine tetraacetic acid.

18. The antimicrobial composition of claim 14, further comprising at least one surfactant.

19. The antimicrobial composition of claim 18, further comprising at least one surfactant selected from the group consisting of an anionic surfactant, a nonionic surfactant, a amphoteric surfactant and any combination thereof.

20. The antimicrobial composition of claim 19, further comprising at least one anionic surfactant selected from the group consisting of an alcohol ether sulfate with 2 to 4 moles of ethoxylation, sodium lauryl sulfate, sodium

α-olefin sulfonate, alkali fatty acid soap, sulfosuccinate, α-sulfomethyl ester, and fatty acylisethionate.

21. The antimicrobial composition of claim 19, further comprising at least one alkyl polyglycoside as the nonionic surfactant.

22. The antimicrobial composition of claim 19, further comprising at least one betaine or at least one amphoacetate as the amphoteric surfactant.

23. The antimicrobial composition of claim 19, further comprising about 1 to about 30 weight percent of the anionic surfactant, about 1 to about 20 weight percent of the nonionic surfactant, and about 0.5 to about 10 weight percent of the amphoteric surfactant.

24. The antimicrobial composition of claim 14, further comprising at least one skin conditioning agent.

25. The antimicrobial composition of claim 14, further comprising at least one thickener.

26. The antimicrobial composition of claim 14, wherein the composition is a liquid.

27. The antimicrobial composition of claim 14, wherein the composition is an aqueous liquid.

28. The antimicrobial composition of claim 14, wherein the composition has a pH of at least 5.0.

29. The antimicrobial composition of claim 28, wherein the composition has a pH ranging from about 5.0 to about 11.0.

30. The antimicrobial composition of claim 29, wherein the composition has a pH ranging from about 7.5 to about 9.5.

31. A method for cleaning skin comprising contacting a the skin with a composition comprising:

(a) a surfactant system selected from the group consisting of an anionic surfactant, a nonionic surfactant, a amphoteric surfactant and any combination thereof; and

(b) the antimicrobial composition according to claim 1.

32. The method of claim 31, wherein the antimicrobial composition comprises:

(a) about 0.2 to about 6.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.2 to about 6.0 percent by weight of 4-chloro-3,5-dimethyl phenol; and

(c) about 0.05 to about 4.0 percent by weight of glutaraldehyde.

33. The method of claim 32, wherein the antimicrobial composition comprises:

(a) about 0.25 to about 4.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.25 to about 4.0 percent by weight of 4-chloro-3,5-dimethyl phenol; and

(c) about 0.1 to about 3.0 percent by weight of glutaraldehyde.

34. The method of claim 31, wherein the surfactant system comprises about 1 to about 30 weight percent of the anionic surfactant, about

1 to about 20 weight percent of the nonionic surfactant, and about 0.5 to about 10 weight percent of the amphoteric surfactant.

35. A method for cleaning skin comprising contacting a the skin with a composition comprising:

(a) a surfactant system selected from the group consisting of an anionic surfactant, a nonionic surfactant, a amphoteric surfactant and any combination thereof; and

(b) the antimicrobial composition according to claim 14.

36. The method of claim 35, wherein the antimicrobial composition comprises:

(a) about 0.2 to about 6.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.2 to about 6.0 percent by weight of 4-chloro-3,5-dimethyl phenol;

(c) about 0.05 to about 4.0 percent by weight of glutaraldehyde; and

(d) about 0.05 to about 6.0 percent by weight of a tetrasodium salt of ethylenediameine tetraacetic acid.

37. The method of claim 36, wherein the antimicrobial composition comprises:

(a) about 0.25 to about 4.0 percent by weight of 2,4,4'-trichloro-2'-hydroxydiphenyl ether;

(b) about 0.25 to about 4.0 percent by weight of 4-chloro-3,5-dimethyl phenol;

(c) about 0.1 to about 3.0 percent by weight of glutaraldehyde; and

(d) about 0.5 to about 4.0 percent by weight of a tetrasodium salt of ethylenediameine tetraacetic acid.

38. The method of claim 35, wherein the surfactant system comprises about 1 to about 30 weight percent of the anionic surfactant, about 1 to about 20 weight percent of the nonionic surfactant, and about 0.5 to about 10 weight percent of the amphoteric surfactant.

INTERNATIONAL SEARCH REPORT

Interr. nal Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/00 C11D3/48 C11D3/20 C11D3/24 A01N35/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C11D A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
4 February 2000	16/02/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Voyiazoglou, D

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Intern. al Application No
PCT/US 99/20179

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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